

- a) a self-replicating origin of replication operative in mammalian cells; and
- b) an LCR ,or component thereof, which, when operatively linked to a gene of interest and present in a mammalian host cell, directs extrachromosomal transcription of said gene in a tissue-restricted manner, wherein said vector replicates extrachromosomally.

27. A DNA expression vector comprising:

- a) a self-replicating origin of replication operative in mammalian cells; and
- b) a β -globin LCR , or component thereof, which, when operatively linked to a gene of interest and present in a mammalian host cell, directs extrachromosomal transcription of said gene in a tissue-restricted manner, wherein said vector replicates extrachromosomally.

28. The vector of claim 27, wherein said vector comprises a component of the LCR.

29. The vector of claim 28 wherein the component of the β -globin LCR consists essentially of HS3.

30. The vector of claim 28 wherein the component of the β -globin LCR excludes HS2.

31. The vector of claim 28 wherein the component of the β -globin LCR consists essentially of HS3 and HS4.

32. The vector of claim 26, wherein the origin of replication is a viral origin of replication.

33. The vector of claim 32 wherein the viral origin of replication is an origin of replication from Epstein-Barr virus.

34. The vector of claim 26, further comprising a sequence encoding a replication factor

required for replication of the expression vector in a host cell.

35. The vector of claim 34 wherein the sequence encoding the replication factor is selected from the group consisting of a sequence encoding EBNA-1 of Epstein-Barr virus, a sequence encoding E1 of papilloma virus, and a sequence encoding E2 of papilloma virus.
36. The vector of claim 26, further comprising an antibiotic resistance gene for selecting cells in culture stably transfected with the expression vector.
37. The vector of claim 26 or 27, further comprising a gene of interest.
38. The vector of claim 37, further comprising a eukaryotic transcription termination sequence between the LCR and the gene of interest and operative to prevent transcription therebetween.
39. A pair of vectors comprising an expression system for expressing a gene of interest in a host cell in a tissue-restricted manner, the pair of vectors comprising:
- i) a first vector comprising
 - (a) an origin of replication operative in mammalian host cells;
 - (b) an LCR, or functional component thereof, which when operatively linked to a gene of interest and present in a mammalian host cell directs extrachromosomal transcription of said gene in a tissue restricted manner; and
 - (c) a gene of interest; and
 - i) a second vector comprising
 - (a) an origin of replication operative in a mammalian host cell; and
 - (b) a sequence encoding a replication protein, said replication protein being necessary for replication of said origin of replication.
40. The pair of vectors of claim 39, wherein the LCR, or component thereof, is a β -globin

LCR, or component thereof.

41. The pair of vectors of claim 39 wherein said first vector comprises a component of the β -globin LCR.
42. The pair of vectors of claim 41 wherein said component of the β -globin LCR consists essentially of HS3.
43. The pair of vectors of claim 42 wherein said component of the β -globin LCR excludes HS2.
44. The pair of vectors of claim 42 wherein said component of the β -globin LCR consists essentially of HS3 and HS4.
45. The pair of vectors of claim 39 wherein said origins of replication are viral origins of replication.
46. The pair of vectors of claim 45, said viral origins of replication are from Epstein-Barr virus.
47. The pair of vectors of claim 39 wherein the sequence encoding the replication factor is selected from the group consisting of a sequence encoding EBNA-1 of Epstein-Barr virus, a sequence encoding E1 of papilloma virus, and a sequence encoding E2 of papilloma virus, and a sequence encoding E2 of papilloma virus.
48. The pair of vectors of claim 39, wherein each of said first and second vector further comprises an antibiotic resistance gene for selecting cells in culture stably transfected with the expression vector.
49. The pair of vectors of claim 39 wherein said first vector further comprises a

eukaryotic transcription termination sequence placed between the LCR and the gene of interest.

50. A method for expressing a gene of interest in cells of a specific tissue-type comprising administering the vector of claim 26 to a mammal.
51. A method for expressing a gene of interest in cells of a specific tissue-type comprising administering a pair of vectors of claim 39 to a mammal.
52. A method of obtaining persistent, tissue-specific expression of a gene of interest in a host cell in culture, comprising culturing a host cell transfected with the vector of claim 26.
53. A method of obtaining persistent, tissue-specific expression of a gene of interest in a host cell in culture, comprising culturing a host cell transfected with the pair of vectors of claim 39.
54. A method of identifying an LCR or component thereof which when comprised in a non-integrating DNA expression vector, operatively linked to a gene of interest, and present in a host cell, directs expression of said gene in a tissue-restricted manner, comprising:
- i. testing the LCR or component thereof by transfecting a non-integrating vector containing the candidate LCR or component thereof operatively linked to a marker gene into a cell line in which the LCR when integrated is active and also into a cell line in which the LCR when integrated is inactive; and
 - ii. identifying the LCR or component which is only active in the cell line in which the LCR when integrated is active. --

REMARKS

Claims 1, 3-21, 23, and 25 were pending. All pending claims were rejected in the